

Remarks

Applicants respectfully request reconsideration of the rejections set forth in the Office Action mailed on December 17, 2002. Claims 60-67 have been withdrawn from consideration. Claims 31 and 50 have been rejected. Claim 51 has been objected to. Claim 51 has been rewritten in independent form and re-presented as Claim 68. Claims 69-76 have been added. Support for the new claims can be found at, for example, Figure 2 and pages 17 and 39.

Applicants note with appreciation that the rejections under 35 U.S.C. §112, first and second paragraphs, the double patenting rejection, and the rejections under 35 U.S.C. §102 based on Kazhevnikov and Debnath have been withdrawn.

The comments in the Office action are now addressed in turn.

Withdrawal from Consideration

The Examiner has withdrawn Claims 60-67 from consideration. The Examiner has provided no proper reasons for the withdrawal. Applicants respectfully traverse.

For a withdrawal from consideration to be proper, the claim groups identified must be independent or distinct from one another. In addition, examining all claim groups in a single application must present a serious burden on the Examiner.

Claim 60 and 64 drawn to a composition comprising a pharmaceutically acceptable excipient and a quinazolinone compound of Claim 31 or 50, respectively. Claims 61-63 and 65-67 provide for the inclusion of other chemotherapeutics (i.e., a taxane, a vinca alkaloid or a topoisomerase I inhibitor) in the composition.

The current Office Action states in paragraph 4 that the cited Chenard reference does not disclose a pharmaceutical composition comprising a vinca alkaloid or topoisomerase I inhibitor in combination with a quinazolinone compound as claimed herein.

Applicants respectfully maintain that it can be inferred from this statement that the Office has, in fact, already reviewed and searched at least Claims 60, 62, 63, 64, 66, and 67. As such, Applicants respectfully maintain that it would not place an undue burden on the Examiner to include Claims 60-67 with the other pending claims in this case. Applicants respectfully request that Claims 60-67 be rejoined with the pending claims.

Rejections under 35 U.S.C. § 112

New Matter

Claim 31 has been rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. More specifically, the Examiner maintains that there is no support for a quinazolinone compound with R₄ as "heterocyclyl". Applicants respectfully disagree. Support for this substituent can be found, for example, at page 17, lines 27-28. Applicants believe that the Examiner's concerns have been addressed. Applicants request that the rejection be withdrawn.

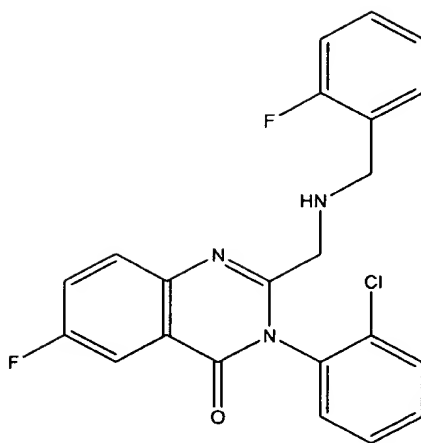
Rejections under 35 U.S.C. §102(b) / (e)

Claims 31 and 50 have been rejected as being allegedly anticipated by Chenard et al. EP 884,310 or EP 900,568 or U.S. '812 ("Chenard"). The rejection is respectfully traversed as applied to the amended claims.

As repeatedly indicated by the courts, anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. There must be no difference between the claimed invention and the disclosure provided by the reference, as viewed by a person of ordinary skill in the field of the invention. (*Scripps Clinic & Research Fdn. v. Genentech, Inc.*, 927 F.2d 1565, 1576 [Fed. Cir. 1991]). Furthermore, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. (*In re Royka*, 490 F.2d 981, 180 USPQ 580 [CCPA 1974]).

The present invention is drawn to various quinazolinone amines. As claimed herein, these compounds have a stereogenic center at the carbon to which R₂ and R₂' are attached. More specifically, R₂ and R₂' are different. As they are different, the stereogenic center is chiral. In a preferred embodiment, the stereogenic center is of the R-configuration.

Chenard describes a quinazolin-4-one core structure having a substituent of the formula –Y-Z-(BR³R⁴) wherein Y-Z can be either –CH₂NH- or –NHCH₂- and B is phenyl, pyridyl, or pyrimidyl. More specifically, the Office has cited Chenard for its description of the compound of Example 10 of EP '310 (i.e., 3-(2-chlorophenyl)-6-fluoro-2-[(2-fluoro-benzylamino)-methyl-3H-quinazolin-4-one):



Applicants respectfully maintain that neither the Chenard compound nor the generic structure of Chenard anticipate the claimed invention. As noted previously and above, Chenard requires that Y-Z be either $-\text{CH}_2\text{NH}-$ or $-\text{NHCH}_2-$. In other words, Chenard describes compounds with hydrogen as both R_2 and R_2' (using the nomenclature system of the current application). Likewise, the cited Chenard compound bears a $-\text{CH}_2-$ moiety. Chenard does not teach or suggest any compounds that have different R_2 and R_2' groups, as claimed herein.

The Office maintains that it does not matter whether the R_2 and R_2' groups are the same or not. Applicants disagree and respectfully maintain that it does matter whether the substituents on the carbon “are the same or not”.

More specifically, as noted above, the presence of the differing R_2 and R_2' groups in the compounds claimed herein gives rise to a *chiral* carbon. Applicants would direct the Examiner to the enclosed copy of page 105 of *Introduction to Organic Chemistry* by Streitwieser and Heathcock, Macmillan Publishing Co., Inc. (1976) which states that “[a]n object that is not superimposable upon its mirror image is chiral.” Applicants would also direct the Examiner to the online dictionary at <http://cancerweb.ncl.ac.uk/omd/> which defines “chiral” as “a term used to describe a molecule which, in a given configuration, cannot be superimposed on its mirror image.” To reiterate, the compounds claimed herein, wherein R_2 and R_2' are different, are not superimposable upon themselves and thus, are chiral.

Moreover, as noted in the specification, Applicants have found that the presence of the chiral center has a significant effect on the activity of the compounds. Specifically, Applicants have found that the R-isomer is dramatically more active than the S-isomer.

Careful inspection of the above Chenard compound reveals that it is superimposable upon its mirror image and thus, is achiral. It is not, as the Examiner contends, a racemate. Chenard does not teach or suggest any quinazolinone amines having different R₂ and R_{2'} groups, as claimed herein. Chenard does not teach or suggest any chiral quinazolinones. Applicants submit that Chenard does not teach every element of the claims; therefore, that the invention, as claimed herein, is not anticipated by Chenard.

Rejections under 35 U.S.C. § 103

Claims 31 and 50 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard '310. Chenard is cited as above.

As discussed above, the claimed invention focuses on a embodiment of the invention wherein the compounds have a chiral center and/or selected substituent patterns at R₁ or R₄. The cited reference does not teach or suggest these limitations. Applicants respectfully request that the rejection be withdrawn.

Claim Objections

Applicants acknowledge with gratitude the indication by the Office that Claim 51 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have amended Claim 51 accordingly. Applicants request that the objection be withdrawn.

Information Disclosure Statement

As the Office has correctly noted, there was a typographic error in Applicants' IDS of September 4, 2002 (received by the Office September 10, 2002). Indeed, the IDS should have had only one page. Applicants apologize for any inconvenience this inadvertent error caused the Office.

In addition, copies of the references were not provided pursuant to 37 C.F.R. §1.98(d). However, as the Office seems to be having difficulty locating the file for the parent application, copies of the cited references are enclosed herewith. Applicants request that the references be made of official record in this application.

Finally, the IDS of September 23, 2002 (received by the Office September 30, 2002) includes various listings from catalogs. Applicants wishes to have considered the compounds specifically tabulated in the listings provided to the Office (i.e., the two compounds from the Maybridge catalog (Reg. Nos. 288844-03-1 and 39070-48-9); the 11 compounds that were

commercially available from Comgenex; and the various commercial compounds from various sources.) Applicants request that these references be made of official record in this application.

Conclusion

The Applicant respectfully maintains that all pending claims are in condition for allowance. Therefore, the Applicant respectfully requests a Notice of Allowance for this Application from the Examiner. Should any unresolved issues remain, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,
BEYER WEAVER & THOMAS, LLP

A handwritten signature in black ink, appearing to read "Lauren L. Stevens", with a stylized flourish at the end.

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